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Abstracts
S14 Bioenergetics of Prokaryotes

Lectures

14L.1 Thermodynamic and kinetic properties of Na^+-motive NADH: Quinone oxidoreductase

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The Na^+-translocating NADH:quinone oxidoreductase (Na^+-NQR) is a component of the respiratory chain of various bacteria. This enzyme is an analogous but not homologous counterpart of mitochondrial Complex I. Na^+-NQR drives the same chemistry and also uses released energy to translocate ions across the membrane, but it pumps Na^+ instead of H^+. The study of H^+-pumps is hampered by the complexity of separation between protons taking part in the catalytic redox reactions and the protons involved in the transmembrane translocation process (pumping). From that point of view, the investigation of the redox-driven *sodium* pump gives a unique possibility to separate these ions, because in this case the redox chemistry still requires protons, but the translocation activity depends only on the presence of Na^+. For example, for sodium-translocating enzymes it is possible to resolve the events of the catalytic cycle, which are slowed down at low concentrations of the coupling ion. This approach reveals the specific transitions of the catalytic cycle responsible for the sodium translocation. On the other hand, study of the dependence of the thermodynamic properties of a sodium pump on Na^+ concentration allows determination of the mechanism of conversion of the redox energy into the sodium-motive force. The report will be devoted to modern knowledge on the structural and catalytic characteristics of Na^+-NQR and focused on the sodium dependence of the kinetic and thermodynamic properties of the enzyme.

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14L.2 Electron transfer activity through the quinone-binding site of complex II (succinate: Quinone reductase)

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Complex II (succinate–quinone reductase) is part of the mitochondrial and bacterial respiratory chain. The enzyme complex is composed of a hydrophilic dehydrogenase domain composed of the SdhA (flavoprotein) and SdhB (iron–sulfur protein) subunits. The SdhAB subunits are bound to the membrane by two hydrophobic subunits SdhC and SdhD which also form the site for attachment of the heme *b*. There are two spatially separated catalytic sites in complex II; one is the dicarboxylate binding site in SdhA where succinate oxidation occurs and the other is in the hydrophobic domain where quinone-reduction takes place. The two catalytic sites communicate with each other through a series of three iron–sulfur clusters in the SdhB subunit. Conserved amino acid residues from the SdhB, SdhC, and SdhD subunits are involved in binding and stabilizing the quinone. Mutation of one of these amino acids, SdhB His207, results in changes in the redox properties of the [3Fe–4S] cluster proximal to the quinone binding site. The structure of the SdhB His207Thr mutant enzyme suggests that alteration of the hydrogen-bonding pattern of the [3Fe–4S] cluster results in the lowering of the redox potential of the iron–sulfur cluster. The mutant enzyme is still able to bind quinones although there is about a 30% reduction in steady state turnover activity. Electron transfer to the heme in the mutant enzyme is altered by comparison with wild-type and the SdhD His71Gln mutant enzyme. The latter has a lowered redox potential for the heme *b*. The data suggest altered pathways for heme reduction in wild-type and mutant enzymes.

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14L.3 Energetics of mycobacteria: A fertile area for new anti-TB drugs

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Current tuberculosis (TB) treatment regimes depend on four front-line anti-TB drugs: isoniazid, pyrazinamide, rifampin and ethambutol, all developed in the 1950s–1960s. Coupled with the slow growth of *Mycobacterium tuberculosis* (generation time about 24 h), means that chemotherapy is prolonged; current "short course" treatment requires multi-drug therapy for 6–9 months. New drugs are urgently needed, to shorten this period, to address persistence, and to deal with the increasing incidence of multi- and extensively-drug resistant TB. An area that is starting to attract considerable interest for drug development is the metabolism and bioenergetics of *M. tuberculosis* during persistence with the realization that the entry into a persistent state is largely a metabolic phenomenon. ATP generation by the membrane-bound F_1F_O-ATP synthase is essential for growth and persistence in mycobacter-

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